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Dentigerous Cyst with Ameloblastomatous And CEOT-like Changes: A Rare Occurrence

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Abstract

A dentigerous cyst is a developmental odontogenic cyst that encases the crown of an unerupted tooth and is attached at the cementoenamel junction. It is 2nd most common cyst of the jaws which comprises 20 % of odontogenic cysts. Most of the reported cases are from the 2nd to 3rd decade of life. It is usually associated with mandibular third molars and maxillary canines, which are more likely to be impacted in adolescents and young adults. Here, we are reporting a case of an ameloblastoma that arose in the wall of a dentigerous cyst. The clinical, radiographic, and histological characteristics were similar to those of dentigerous cysts, as were seen on doing an incisional biopsy. Enucleation was done intraorally under local anesthesia. Post-operative excisional biopsy revealed strands and cords arising from the cystic lining, which are suggestive of ameloblastic changes along with calcification, and amyloid deposits resembling CEOT-like changes in the layers of the connective capsule.

Keywords: Dentigerous cyst, Ameloblastoma, CEOT, Calretinin, Amyloid

Introduction

Out of all odontogenic cysts of jaws, approximately 20% were dentigerous cysts.[1] Commonly occurring in the mandibular third molar followed by maxillary canines, mandibular premolars, maxillary third molars, and supernumerary teeth.[2] The male: female ratio was 1.7:1.[3] Patients generally complain of painless swelling.[4] The neoplastic transformation is highest in the radicular cyst followed by the dentigerous cyst and then the Odontogenic keratocyst.[6] The prognosis of dentigerous cyst is excellent but this cyst might undergo neoplastic transformation into ameloblastoma/squamous cell carcinoma/mucoepidermoid carcinoma. In this case report, we have studied the lining wall of the dentigerous cyst which has shown ameloblastomatous transformation along with sporadic calcification in the deeper layers of the connective capsule. This type of calcification rarely occurs with the dentigerous cyst.[6]

Case Report:

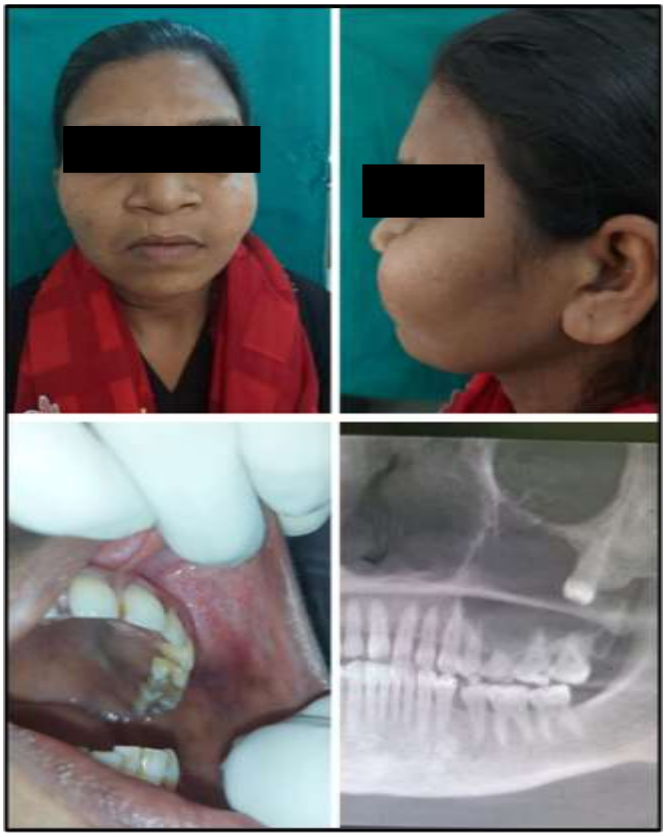
A 20-year-old female patient reported painless swelling on the left side of the face. The swelling was asymptomatic for one year which gradually increased in size and experienced pain for 10–15 days.

On extraoral examination, a solitary diffuse swelling was seen on the left middle third of the face, measuring approximately 2 × 3 cm in size, extending anteriorly from the left corner of the mouth to 3 cm away from the left angle of the mandible, superior-inferior extent was from inferior border of the left eye to left commissure of the mouth, on palpation, the swelling was firm to hard in consistency and non-tender. The temperature & color of the skin overlying the swelling were normal (Figure 1A, B).

Intraoral examination revealed over-retained 65. A firm swelling measuring about 2cm × 1cm was presently associated with 65 showing buccolingual cortical expansion and obliteration of the buccal vestibule. Grade 1 tooth mobility was present with over-retained 65 (Figure no.1 C).

Figure No. 1-

1. Extra-oral swelling extending superio-inferiorly from inferior border of the left eye to left commissure of the mouth.
2. Extraoral swelling extending medio-laterally from left corner of the mouth to 3 cm away from the left angle of the mandible.
3. Intra-oral swelling associated with 65 showing buccolingual cortical expansion and obliteration of the buccal vestibule.
4. CBCT showing single, well-defined, circular unilocular radiolucency with a corticated border extending from 23 to 27 and cystic lesion seen attached to CEJ of impacted 25.



Aspiration biopsy, approximately 4 ml of slight blood-tinged straw-colored fluid, smear examination of the fluid showed RBCs, pus cells, and few cholesterol crystals. A Cone beam computed tomography revealed a single, well-defined, circular unilocular radiolucency with a corticated border in the posterior region of the right maxilla extending from 23 to 27. The cystic lesion seen attached to CEJ of impacted 25. The floor of the left maxillary sinus is elevated superiorly till orbital floor. Loss of buccal cortical plate was evident in association with 65. External root resorption was present with 65. There was also an over-retained 85 and congenitally missing 18,28,38,48 and 45(Figure no.1 D).

A provisional diagnosis of the Dentigerous cyst was given on the basis of clinical, radiographical, and aspiration findings.

The patient underwent an incisional biopsy of the cystic lesion. Histopathology revealed the presence of a cystic cavity devoid of the epithelial lining. Adjacent to the cystic cavity connective tissue wall consists of haphazardly arranged collagen fiber bundles with fibroblasts and fibrocytes. Mild to moderate degree of chronic inflammatory cell infiltrate and a mild degree of vascularity with extravasated RBCs was evident. Towards the periphery, osseous trabeculae were seen.

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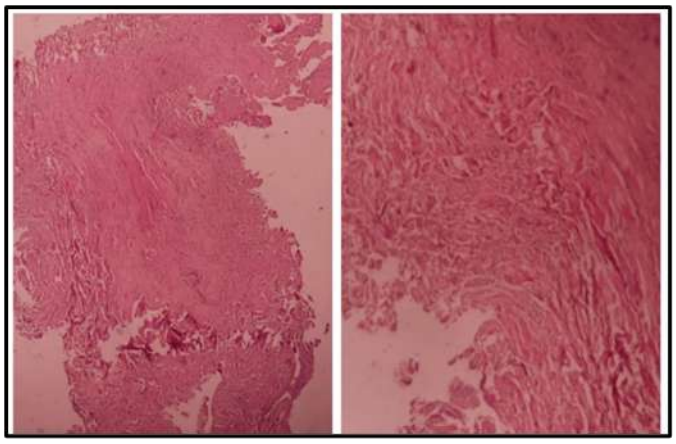
Histopathological examination revealed Secondarily infected Dentigerous cyst (Figure no.2 A,B).

Figure No. 2 –

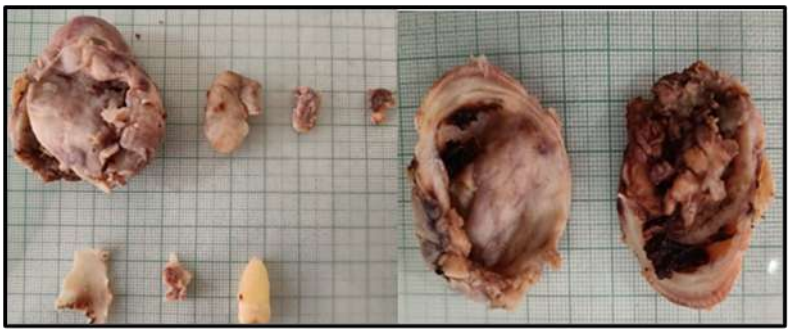
1. Incisional biopsy showing cystic lining devoid of epithelium under 4X
2. Incisional biopsy showing adjacent fibro cellular connective tissue stroma under 10X



Further, under local anesthesia, the lesion was completely excised through an intraoral approach by reflecting mucoperiosteal flap by taking a crevicular incision extending from 23 to 27. Along with enucleation of the cystic lesion extraction of 65 and 25 was done. A gross examination revealed a cystic lesion measuring 5cm 4.5cm 3cm. The cystic wall demonstrated brown-colored irregular nodular thickenings in some areas (Fig.No.3 A,B).

Fig. No. 3 –

1. Received multiple soft tissues, hard tissue, and tooth specimens for histopathological examination.
2. On gross examination cystic wall demonstrates brown colored irregular nodular thickenings



Histopathological examination of the excisional biopsy showed a cystic cavity lined by 2-3 cell layered non-keratinized stratified squamous epithelium. Focally, the pseudo-stratified columnar ciliated epithelium was also present (Fig. No. 4A). The adjacent connective tissue wall towards the lumen was predominantly fibro cellular consisting of a moderate degree of chronic inflammatory cell infiltrate and also showed plenty of odontogenic epithelial islands in the form of strands & sheets of variable sizes.

Focally epithelium was seen proliferating into connective tissue walls as anastomosing strands and cords in a plexiform pattern lined by cuboidal to flatten cells interspersed with loosely arranged stellate reticulum-like cells (Fig.No.4 B). Towards the periphery, the connective tissue wall was predominantly fibrous with parallelly arranged collagen fiber bundles with plump fibroblasts and fibrocytes with osseous trabeculae. A mild degree of vascularity was evident.

Fig.No.4 –

1. Excisional biopsy showing focally lined by pseudo-stratified columnar ciliated epithelium under 10X

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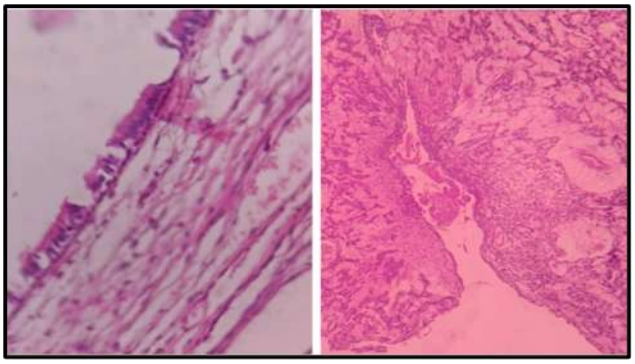
2. Excisional biopsy showing Ameloblastomatous changes in a plexiform pattern under 40 x



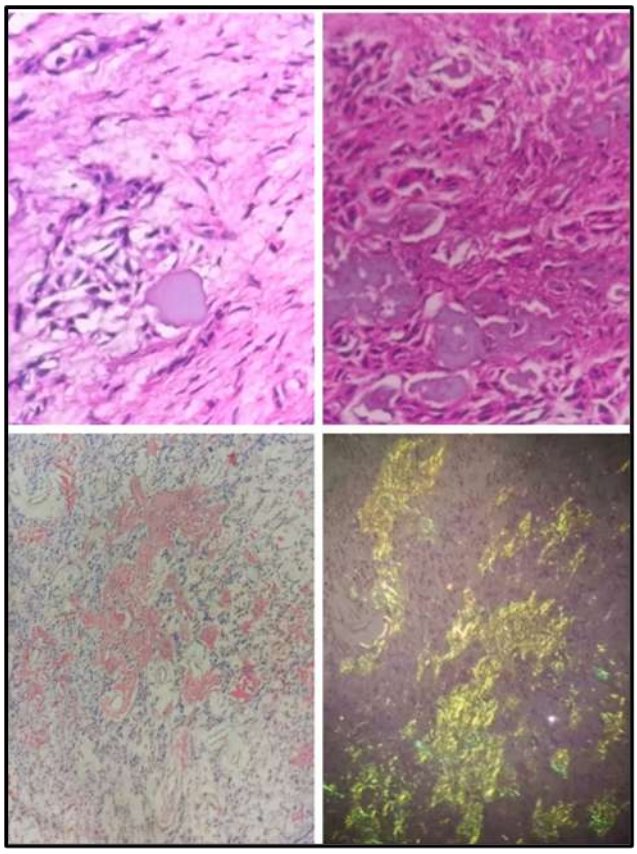
Near capsule, basophilic calcifications of varying sizes were evident (Fig.No.5 A). At a few places amorphous, eosinophilic hyalinized areas are also seen which resemble an amyloid (Fig.No.5 B).

On overall histopathological features, a final diagnosis was given as a Dentigerous cyst with Ameloblastomatous changes along with calcifications.

A special stain like Congo red was also done to confirm areas of amorphous, eosinophilic hyalinized material that stained orange-red colored and gave apple-green birefringence after light polarization (Fig. no. 5 C,D).

Figure No.5 -

1. Basophilic calcifications are seen focally in the H&E stained section under 10X.
2. Amorphous eosinophilic areas are seen in the H&E stained section under 10X.
3. Amorphous eosinophilic hyalinized material showing Redish Orange color on Congo Red staining.
4. On polarized microscopy, amyloid deposits showed Apple Green Birefringence.



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To confirm the histopathological final diagnosis further immunohistochemical analysis was done, which showed Calretinin positive all over in tumor cells and Ki67 proliferative index was noticed 10% (Fig.no.6 A,B).

Figure No. 6 -

1. Odontogenic islands showing Calretinin positive throughout connective tissue stroma
2. Expression of Ki67 positive

Discussion:

Dentigerous cysts (DCs) are one of the most common types of cysts which occur in the jaw. A typical DC clinically presents as an asymptomatic unilocular radiolucency that encloses the crown of an unerupted or impacted tooth. In most of the cases, the diagnosis of a DC is straightforward; but even radiographically, a 'typical' DC can be diagnosed as something else, such as a dental follicle, a hyperplastic dental follicle, an odontogenic keratocyst or a unicystic ameloblastoma on histological analysis.[1] The histological diagnoses of these lesions are therefore critical.[5]

A dentigerous cyst is the most common cause of peri coronal radiolucency which is associated with impacted teeth.[3] Because they are asymptomatic, dentigerous cysts are usually diagnosed on routine dental radiographs. The diagnosis of a dentigerous cyst is based on a combination of radiographic and histopathological features.[4] Dentigerous cysts form within the lining of the dental follicles when fluid accumulates within the follicular epithelium and the crown of a developing or unerupted tooth.[21]

Most dentigerous cysts manifest in the second and third decades of life, with peak incidences in teenagers, as in this case also patient was same age group.[7]

The DC mostly occurs in the mandibular third molar followed by maxillary canines, mandibular premolars, maxillary third molars, and supernumerary teeth but in our case, the cyst was seen in association with the maxillary 2nd premolar which was an unusual finding of this case.[2]

The diagnosis of a dentigerous cyst is based on a combination of radiographic and histopathological features.[8] Dentigerous cysts form within the lining of the dental follicles when fluid accumulates within the follicular epithelium and the crown of a developing or unerupted tooth which was also seen in our case.[9]

An ameloblastoma is a benign and locally aggressive tumor that arises from the mandible or less commonly, from the maxilla. Unicystic ameloblastoma is variants of ameloblastoma, which was first described by Robinson and Martinez, which refer to those cystic lesions that show clinical and radiological characteristics of odontogenic cysts, but which on histological examination, show typical ameloblastomatous epithelium which lines part of the cyst cavity, with or without a luminal or mural tumor proliferation.[10] 15% to 20% of all unicystic ameloblastoma forms in the wall of dentigerous cysts. Since 1925, the development of ameloblastoma within the walls of the odontogenic cyst, among which the most commonly cited were dentigerous cysts as reported.[11]

In our case, there are a few places where epithelium was proliferating into connective tissue walls as anastomosing strands and cords in a plexiform pattern lined by cuboidal to flatten cells interspersed with loosely arranged stellate reticulum-like cells which were similar to Durga Okade et al (2019)[18] and

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Sattya Bhushan et al. (2014)[19]case reports. Cystic degeneration of stellate reticulum-like cells is also evident.

To confirm the histopathological diagnosis of ameloblastomatous changes Immunohistochemical analysis was done by using Calretinin and Ki 67.

Calretinin is regarded as the most extensively expressed calcium-binding protein in central and peripheral neural tissues. This protein may play a vital role during odontogenesis in the formation of enamel. Calretinin also seems to possess a role in the regulation of the expression of growth factors and involvement in cell proliferation, differentiation, and neoplastic transformation. In various studies, calretinin was found to be positive in ameloblastoma only whereas no other tumor or cyst showed positivity.[16,17] Due to calretinin's widespread distribution in many normal and neoplastic human tissues and its presence in the odontogenic epithelium during odontogenesis, it could have also been expressed in cystic and neoplastic odontogenic tissues. All these suggest that calretinin could have some application in the differential diagnosis of odontogenic tumors and cysts. Therefore, further assessment of molecular aspects and immunohistochemical expression of calretinin in neoplastic tissues is essential to provide a better understanding of the biological behavior, influencing factors, and tumorigenesis of odontogenic neoplasms.[13]

In our case also calretinin was found to be positive in all tumor cells which confirms ameloblastomatous changes in the capsule of the dentigerous cyst.

Abnormal cell proliferation is an essential feature of tumorigenesis. Ki-67 is a 319–358 kDa protein, considered a reliable marker for the proportion of proliferating cells and to predict the lesion's behavior. Ki-67 is involved in all the active stages of the cell cycle, but is not present in the resting G0 phase.[14] The immuno-histochemical data on Ki-67 expression in ameloblastomas that arise from dentigerous cysts confirm the hypothesis that ameloblastomas which arise from dentigerous cysts have a biological behavior which is similar to that of unicystic ameloblastomas.[12]

In the present case, Ki67 proliferative index was found 10% which confirms the more aggressive behavior of the lesion as that of the odontogenic tumor which was similar to the Adriano et al study (2002).[20]

In this case, varying amounts of amorphous, eosinophilic amyloid-like material and calcifications were present which were similar to Shreya S Saha et al (2020)[21] and Rashmi J Kurup et al (2022)[22] case reports and the proliferation of a few polyhedral epithelial cells in connective tissue stroma were also present. Confirmation of amyloid-like material deposits was done by Congo red staining and using a polarized microscope. This confirms prominent amyloid-like material and minimal epithelial cells CEOT variant which was an unusual finding in this case. Our case was in cordance with Alexander J.Howie et al study (2009).[23]

CEOT is a rare odontogenic neoplasm that represents about 1% of all odontogenic tumors. It has been proposed that CEOTs originate from the stratum intermedium of the dental organ or from the dental lamina.CEOT can occur at any age; however, it is most often seen between 30 and 50 years of age, with no sex predilection. The vast majority of cases occur in the posterior mandible. CEOT appears clinically as a painless slow-growing mass. Maxillary tumors, however, could be more aggressive, causing symptoms associated with involvement of the nasal cavity, such as stuffiness and epistaxis. Radiographically, CEOTs appear as unilocular or multilocular radiolucencies with or without radiopacities. Approximately 50% of the cases are associated with unerupted teeth and appear radiographically as dentigerous cysts. Histologically, most examples show solid proliferation of polyhedral epithelial cells arranged in discrete islands, strands, or sheets in a background of fibrous stroma with varying amounts of amorphous, eosinophilic, amyloid-like material and calcifications. Other variants of the classic appearance have been recognized and include tumors with (a) minimal amyloid-like material and calcification, (b) prominent amyloid-like material and minimal epithelial cells, and (c) a predominantly clear-cell variant of CEOT.[15]

In this case, there is unusual presentation of three rare odontogenic lesions with distinct overlapping and a combination of histologic features of a combined Dentigerous cyst, Ameloblastoma, and Calcifying epithelial odontogenic tumor. In addition, we

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reviewed the literature and identified there were no such reported cases of odontogenic lesions exhibiting a combination of histologic features. As more of these entities are reported, pathologists will be better able to recognize these lesions. Due to the paucity of cases, the prognosis, clinical behavior, and appropriate treatment of such cases are largely unknown. We hope that as more cases are reported in the literature, a better understanding of combined odontogenic lesions will be obtained.

Conclusion:

It is consequential to determine whether a dentigerous cyst is undergoing any microscopic changes. The histologic features are often identical to other individually well-established odontogenic neoplasms. Their clinical presentation is variable, ranging from cysts to neoplasms showing varying degrees of aggressive behavior. Combined odontogenic neoplasms have rarely been documented. Such tumors have also been described by other researchers as ‘‘hybrid’’ lesions. Many authors believe that hybrid odontogenic lesions are not a result of the collision between two distinct entities but rather due to the pluripotential of the odontogenic epithelium with both lesions likely developing from a common source or ameloblastomatous change in an existing odontogenic cyst. So, the whole cyst should be actively and thoroughly evaluated to rule out any such transformation.

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